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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,604	12/07/2001	Pablo D. Garcia	002441.00008	6543

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,604	GARCIA ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,10 and 13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,10 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed December 27, 2005 in response to the Office Action of June 27, 2005 is acknowledged and has been entered. Claims 1-7, 9-10, 13-15 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

The rejection of claims 1-3, 9-11 and 13-15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn.**

The rejection of claims 1-3, 9-11 and 13-15 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is maintained** for reasons of record. Applicant's arguments have been fully considered but fail to persuade. Applicants' arguments are that HML-2 sequences are known in the art and that the ordinary artisan would know which structure belongs in the HML-2 subgroup.

The instant invention is drawn to (1) a method of diagnosing prostate cancer by detecting an increased level of HML-2 expression product in a sample obtained from the patient prostate, or (2) a method of diagnosing prostate cancer by detecting an increased level of HML-2 expression product in a sample obtained from the patient blood.

Applicants' arguments have been fully considered but fail to persuade. The arguments point to table 11 as providing evidence that there is written description for the HML-2 sequences. The Office does not dispute that HML-2 sequences were known at the time the invention was filed. Merely knowing the sequences of HML-2 does not provide written description for the inventions as claimed. In order to practice the instant invention requires knowledge that a particular HML-2 is associated with prostate tissue and that an increase of that HML-2 transcript is indicative of cancer. The written description rejection is based on the lack of correlation between an increase in any/all HLM-2 sequences as correlating with the presence of prostate cancer. Detecting an increase in HML-2 in blood would not correlate to the presence of prostate cancer. The lack of correlation is evidenced by the observation that "HERV-K family (HML-2) has been reported to be expressed in teratocarcinoma and breast cancer cell lines..... There is no evidence, however, that HERVs are directly implicated in carcinogenesis." (see Stauffer et al. Cancer Immunity (2004) Vol. 4, pp. 1-18, see discussion paragraph 3). "On the other hand, antibody responses against HERV-K (HML-2) proteins have been observed in patients with germ cell tumors. In addition, antibodies reactive against cDNA clones encoding HERV-K (HML-2) Gag or Env were identified in the sera of testicular, melanoma and prostate cancer patients using SEREX methodology, demonstrating that a humoral immune response was mounted against these proteins." (see Stauffer et al. Cancer Immunity (2004) Vol. 4, pp. 1-18, see discussion paragraph 3). This reference provides direct evidence that observing an increase in the level of HML-2 in the serum does not directly correlate with prostate cancer because the increase could also be due to testicular cancer or skin cancer (melanoma).

Detecting SEQ ID NO:155 in a serum sample from a patient would not provide any information regarding the prostate cancer status of the patient, because SEQ ID NO: 155 is from a protein of the R region of the endogenous retrovirus that is found in all full-length HML-2 transcripts. (see specification page 4, lines 13-15).

The art indicates that HML-2 comprises a diverse group of retroelements (Zsiros et al. Journal of General Virology, 1998, listed on IDS; see figures) having diverse structures at the nucleic acid level. The art has not correlated an increased HML-2 occurrence to any disease stage. HERV-K (HML-2) is expressed in normal tissue as well as cancerous tissue (see table 2, Stauffer et al. Digital expression profiles of human endogenous retroviral families in normal and cancerous tissues. Cancer Immunity (2004) Vol. 4, pp. 1-18). Because the expression can occur in both cancerous and normal tissue, an increase in expression will not correlate with a diagnosis of any kind of disease. A diagnosis could only be made with those sequences for which such a correlation has been established and would be limited to those specific sequences. The HERV-K (HML-2) family is expressed in normal muscle tissue and is overexpressed in normal brain, skin and pancreas as well as in cancers of the brain, head and neck, uterus. The level of EST expression of HERV-K 22q11 (HML-2) is higher in normal prostate tissue than in prostate cancers (see table 2, Stauffer et al., 2004, page 12, 2nd paragraph). Therefore, only the isolated polynucleotide sequences that have actually been correlated with prostate cancer meet the written description provision of 35 U.S.C. §112, first paragraph.

The rejection of claims 1-7, 9-11 and 13-15 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention **is maintained** for reasons of record.

Applicants assert that the office has not provided any evidence to doubt that HML-2 variants will predictably associate with prostate cancer. In response, detecting an increase in HML-2 in blood will not correlate with the presence of prostate cancer because HML-2 is found expressed in many tissues and is found in many different cancers. "HERV-K family (HML-2) has been reported to be expressed in teratocarcinoma and breast cancer cell lines..... There is no evidence, however, that HERVs are directly implicated in carcinogenesis." (see Stauffer et al. Cancer Immunity (2004) Vol. 4, pp. 1-18, see discussion paragraph 3). "On the other hand, antibody responses against HERV-K (HML-2) proteins have been observed in patients with germ cell tumors. In addition, antibodies reactive against cDNA clones encoding HERV-K (HML-2) Gag or Env were identified in the sera of testicular, melanoma and prostate cancer patients using SEREX methodology, demonstrating that a humoral immune response was mounted against these proteins." (see Stauffer et al. Cancer Immunity (2004) Vol. 4, pp. 1-18, see discussion paragraph 3). This reference provides direct evidence that observing an increase in the level of HML-2 in the serum does not directly correlate with prostate cancer because the increase could be due to testicular cancer or skin cancer (melanoma).

The instant invention is drawn to (1) a method of diagnosing prostate cancer by detecting an increased level of HML-2 expression product in a sample obtained from the patient prostate, or (2) a method of diagnosing prostate cancer by detecting an increased level of HML-2 expression product in a sample obtained from the patient blood. The specification has shown that an increase in the HML-2 level in prostate tissue correlates with prostate cancer (see

specification page 37, line 10-16 and table 6). This correlation is limited to analyzing prostate tissue samples. Neither the specification nor the art support the claims drawn to detecting HML-2 in blood and associating the HML-2 increase with prostate cancer, because antibodies reactive against cDNA clones encoding HERV-K (HML-2) Gag or Env were identified in the sera of testicular, melanoma and prostate cancer patients using SEREX methodology, demonstrating that a humoral immune response was mounted against these proteins." (see Stauffer et al. Cancer Immunity (2004) Vol. 4, pp. 1-18, see discussion paragraph 3). Thus, the Office has provided evidence to doubt applicants' inventions as claimed.

In response the art indicates that HML-2 comprises a diverse group of retroelements (Zsiros et al. Journal of General Virology, 1998, listed on IDS; see figures) having diverse structures at the nucleic acid level. The art has not correlated an increased HML-2 occurrence to any disease stage. HERV-K (HML-2) is expressed in normal tissue as well as cancerous tissue (see table 2, Stauffer et al. Digital expression profiles of human endogenous retroviral families in normal and cancerous tissues. Cancer Immunity (2004) Vol. 4, pp. 1-18). Because the expression can occur in both cancerous and normal tissue an increase in expression will not correlate with a diagnosis of any kind of disease. A diagnosis could only be made with those sequences for which such a correlation has been established and would be limited to those specific sequences. The HERV-K (HML-2) family is expressed in normal muscle tissue and is overexpressed in normal brain, skin and pancreas as well as in cancers of the brain, head and neck, uterus. The level of expression of HERV-K 22q11 (HML-2) is higher in normal prostate tissue than in prostate cancers (see table 2, Stauffer et al., 2004, page 12, 2nd paragraph). Because an observation in the increased level of an endogenous HML-2 retrovirus in a blood

sample does not directly correlate with any specific cancer the instant invention is rejected as not being enabled for the full scope of the invention as claimed.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PH.D.
PRIMARY EXAMINER 3/17/06